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Baxter

December 2, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: *Federal Register* Notice August 19, 1999 (FR Vol. 64, No. 160. p45375)
Docket No. 98N-0673

Dear Colleague:

Baxter Healthcare Corporation, Fenwal Division is submitting comments on the proposed rule *Revisions to the Requirements Applicable to Blood, Blood Components, and Source Plasma; Companion Document to Direct Final Rule* published on August 19, 1999 in the *Federal Register.*

The following are our comments:

1. Currently, due to the solution components contained in our manual blood collection, processing and storage systems (i.e., Fenwal Blood-Pack@ Units), these products are cleared for market entry under New Drug Applications (NDA) and are considered "drugs", We have noticed that the word "device(s) is used throughout this proposed rule in reference to following timeframes specified in directions for use. Please clarify whether this proposed rule is only applicable to blood collection, processing and storage systems that are regulated as "devices" or, will the premarket FDA clearance path for manual blood collection, processing and storage systems change from NDA to 5 1 O(k) Premarket Notifications in the future.

2. In the proposed rule under $640, the requirements for blood and blood component processing/preparation currently specified in the CFR are to be replaced with "within the timeframe specified in the directions for use of the specific device". Many of the processing and separation time and temperature requirements in the current version of §640, while not manufacturer's approved indications, are well-established industry practices versus approved indications. We propose retaining the language currently found in the CFR, and allowing some flexibility by adding the phrase "or within the timeframe specified in the directions for use of the specific device." In this way, if a

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manufacturer has no additional intended use specific to their product, no additional text would need to be included in their directions for use.

As an example, we would propose §640.34 to read as follows:

(c) Liquid Plasma. Liquid plasma shall be separated from the red blood cells within 26 days after phlebotomy (within 40 days after phlebotomy when CPDA- 1 solution is used as the anticoagulant) and shall be stored at a temperature of 1 to 6°C within 4 hours after filling the final container, or within the timeframe specified in the directions for the use of the specific device.

3. In the proposed rule under §640.34(b), §640.34(e) and §640.54(a), there is use of the term "frozen solid". We propose replacing this term with "placed in the freezer". Please see CPG 7 134.20, Section 23 1.120 where it states *"Based on recommendations receivedfrom the Panel on Safety and Efficacy of Blood and Blood Derivatives, the Center for Biologics Evaluation and Research is preparing to modify the regulation to indicate that: a. The 4-hour periodfor separation of plasma from red cells be changed to 6 hours (Please note-The plasma should be placed in the freezer within 6 hours. 21 CFR 640.34(b), which requires that plasma be frozen solid within 6 hours will be revised to reflect this change)."*

4. The above referenced Compliance Policy Guide (CPG 7134.20) states that 21 CFR 640.34(b) would be modified to indicate that *"Platelets may bepreparedfrom platelet-rich plasma at any time during the dating period assigned to platelets, provided that 1) Not more than 6 hours following collection of whole blood, the red cells are separatedfrom the platelet-rich plasma and refrigerated; and 2) The platelet-rich plasma is stored at the appropriate temperature (20-24°C) until the platelets are separated."* We agree that this information needs to be incorporated into the CFR. We propose adding this modification to the CFR by way of including it in the subject proposed rule.

5. Upon review of the proposed/final rule as currently written, it is clear that detailed requirements for a number of product usage practices and procedures associated with blood component collection and processing would be moved from 21 CFR 640 to drug/device product labels. It should be made clear by the Agency that blood component manufacturing practices and procedures performed by blood centers using currently approved drug and device products will be transposed by manufacturers to product labeling without additional Agency review as of the effective date of the rule implementation.

6. Regarding the effective date for implementation of this proposed/final rule, it should be pointed out that the rule as currently written would place extreme burden and hardship on manufacturers of manual blood collection, processing and storage systems. As is the case in all situations that affect large product inventories, any transition must be managed in such a way as to allow existing product inventory to be used until supplies are exhausted. Fenwal estimates that a transition period to make major modifications to our labeling would need to be implemented over a 2-3 year period.

7. If this proposed rule is adopted as written in the referenced *Federal Register* notice, without the above referenced modifications, FDA should then consider our statements in this letter as "adverse comments".

Should you have questions regarding this letter please contact me at (847) 270-4294 or Daphne Maurer at (847) 270-4979.

Sincerely,

for Daphne Maurer

Steven B. Binion, Ph.D.
Vice President Regulatory Affairs
Fenwal Division